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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 56029-40434	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US03/11802	International filing date (day/month/year) 15 April 2003 (15.04.2003)	Priority date (day/month/year) 15 April 2002 (15.04.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): A01N 63/00; C12N 1/20 and US Cl.: 424/234.1, 257.1, 258.1, 93.1, 93.2, 93.4; 435/243, 252.3		
Applicant WASHINGTON UNIVERSITY		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>6</u> sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input checked="" type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input checked="" type="checkbox"/> Certain observations on the international application</p>		
Date of submission of the demand 29 October 2003 (29.10.2003)	Date of completion of this report 29 October 2004 (29.10.2004)	
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Patricia A. Duffy <i>P. Roberts for</i> Telephone No. (571) 272-1600	

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US03/11802

I. Basis of the report

1. With regard to the elements of the international application:*

- ☐ the international application as originally filed.
- ☒ the description:
pages 1-72 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☒ the claims:
pages NONE, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages 73-78, filed with the letter of 16 July 2004 (16.07.2004).
- ☒ the drawings:
pages 1-54, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.
- ☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 2-4,7, 28 and 33-40

because:

☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 2-4,7,28 and 33-40

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/11802**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

Novelty (N)	Claims <u>NONE</u>	YES
	Claims <u>1, 5, 6, 8-27, 29-32</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1, 5, 6, 8-27, 29-32</u>	NO
Industrial Applicability (IA)	Claims <u>1, 5, 6, 8-27, 29-32</u>	YES
	Claims <u>NONE</u>	NO

2. CITATIONS AND EXPLANATIONS

Neither of the priority documents discloses the claimed invention to enable the claims using an attenuated derivative of a pathogenic *Salmonella* species that has an enhanced ability to produce cross-protective immunity for the family of *Salmonella* species and *E. coli* strains. The disclosure is limited to a single *Salmonella typhimurium* with specific mutations in specific genes. The priority documents lack written description of cross-protection studies using the disclosed attenuated *Salmonella typhimurium* with a number of different genera encompassed within the claimed *Salmonella* genus and *E. coli* species. As such, the priority has been found to be invalid.

Claims 1, 5, 6, 8-27 and 29-32 lack novelty under PCT Article 33(2) as being anticipated by Zhang et al. (Abstracts of the General Meeting of the American Society for Microbiology, May 2, Vol. 102, pages 512-513, Abstract).

Zhang et al teach strains of *Salmonella typhimurium* that has delta pm1-2426 and delta fur::araC pBADfur deletion mutations that have cross-protectivity against other *Salmonella* serotypes. The amendment presented in the letter of 16 July 2004 does not obviate this objection.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claim 1 and every claim dependent thereon are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claim 1 is indefinite for the following reason(s): the claims recite "a first antigen antigen", "a first carbohydrate antigen" and a second carbohydrate antigen". It is unclear how the first antigen is related to the "first carbohydrate antigen". The but fail to define "a first antigen" as such, it is unclear what is the first antigen. The claim recites multiple means for regulatable expression and in the means of step (a) a first antigen is set forth while step (b) recites a "first carbohydrate antigen". It is unclear what is first, second and third. It is unclear what is regulated and the nature of the antigen as it relates to the means. Therefore, the claims are still confusing and the amendment filed with the letter of 16 July 2004 does not obviate this issue.

Claims 1, 5, 6, 8-27, 29-32 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because of the claims are not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because: The disclosure is devoid of any showing of enhanced cross-protective immunity using the disclosed attenuated *Salmonella typhimurium* consisting essentially of a Δ fur::TTaraCP_{BAD} *fur* deletion-insertion mutation and a Δ tpm1 mutation. The description lacks written description of enhanced cross-protective immunity toward the genus of *Salmonella* and *E. coli* species as claimed. While the art has documented cross-protection within the genus of *Salmonella* for particular antigens, this description fails to demonstrate induced cross-protection within either this genus or the claimed *E. coli* species. Therefore, the description fails to support by way of written description that the skilled artisan practicing even the particular species disclosed can achieve family related cross-protection for pathogenic bacteria falling within the family regardless of the particular genus and species.

In view of the lack of written description of the ability of any attenuated bacterium of the disclosure to induce enhanced cross-protective immunity against the claimed genus and *E. coli* species using any disclosed attenuated bacterium, the description does not disclose the claimed invention in a manner sufficiently clear to be carried out by a person skilled in the art.